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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460
OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION
OFFICE OF PESTICIDE PROGRAMS REGISTRATION DIVISION (7505P)

DOCUMENT CONTAINS CONFIDENTIAL BUSINEES INFORMATION

DP BARCODE No.: D457776; **FILE SYMBOL/REG. No**.: 5481-647(AltCSF#2); **PRODUCT NAME**: Quizalofop P-ethyl Technical; **DECISION No**.: Not provided; **PC Code(s**): 128709; **ACTION CODE**: R351; **FOOD Use**: Yes

DATE: January 28, 2021

SUBJECT: Product Chemistry Review of "Quizalofop P-ethyl Technical"

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REGISTRANT: AMVAC Chemical Corporation

MRID Number(s): 51096401, 51096402

INTRODUCTION:

The registrant has submitted an application requesting approval of the amendment to add a new unregistered source of active ingredient for the technical grade product "Quizalofop P-ethyl Technical" (EPA Reg. No. 5481-647). The new manufacturer (Alternate Source #2) is [redacted]

In support of the application, the registrant has submitted Group A product chemistry data with MRID Nos. 51096401 and 51096402. The proposed Alternate CSF #2 (dated 04/02/2020) for Alternate Formulation #2 was also submitted for the product. CITAB has been asked to determine the acceptability of the product chemistry data and proposed Alternate CSF #2. The registrant submitted the revised alternate CSF #2(dated 01-05-2021) in order to correct the certified limits of the active ingredient. The primary review was performed by Summitec Corporation of Knoxville, TN

SUMMARY OF FINDINGS:

1. Group A guidelines:

830.1550: (product identity & composition)

The active ingredient was adequately described (MRID No. 51096401). The nominal concentration of the active ingredient (96.24%) provided on Alternate CSF #2 (dated 04/02/2020) is the same as the average derived from the five-batch preliminary analysis results (see p. 42 in MRID No. 51096402). The currently approved Basic CSF was not available to the reviewer, so it could not be verified that the active ingredient content listed on Alternate CSF #2 is within the certified limits stated on the currently approved Basic CSF.

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830.1600: (description of materials used to produce the product)

Safety Data Sheets (SDSs) for the starting materials, and their suppliers and specifications were provided in MRID No. 51096401. The product chemistry data submitted for Guideline 830.1600 satisfy the data requirements of 40 CFR §158.325.

830.1620 (description of production process)

A description of the production process, chemical pathways, equipment used and flow charts were provided in MRID No. 51096401. The product chemistry data submitted for Guideline 830.1620 satisfy the data requirements of 40 CFR §158.330.

830.1670 (discussion on the formation of impurities)

The process-related impurities were identified and quantified as part of the five-batch preliminary analysis (MRID No. 51096402). [redacted] impurities were found to be present at average concentrations ≥ 0.1% w/w. The formation of these impurities was fully discussed in MRID No. 51096401. There is one impurity of toxicological significance in Quizalofop P-ethyl Technical. It was found to be present at a level below the limit permitted by European Food Safety Authority (EFSA).

The product chemistry data submitted for Guideline 830.1670 satisfy the data requirements of 40 CFR §158.340.

830.1700 (preliminary analysis)

The five-batch preliminary analysis of Quizalofop P-ethyl Technical was conducted by Nutrichem Laboratory Co., Ltd. (No. 27, Life Science Park Road, Changping District, Beijing 102206, P.R. China). The content of the active ingredient was determined by using HPLC-UV with external standard calibration, which was validated with respect to system suitability, specificity, linearity, precision and accuracy (MRID No. 51096402). The concentrations of the active ingredient in the five batches were: 96.5, 95.9, 96.4, 96.2, and 96.2% w/w (average 96.24% w/w, from p. 42 in MRID No. 51096402). It is not clear if these concentrations are within the certified limits listed on the currently approved Basic CSF as it was not available to the reviewer. Certificates of analysis for the five batches were provided in MRID No. 51096402.

The product chemistry data submitted for Guideline 830.1700 satisfy the data requirements of 40 CFR §158.345.

830.1750 (certified limits)

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Wider upper certified limit was proposed for the active ingredient, but no justification was provided. The registrant did not propose upper certified limits for the impurities. The nominal concentrations for the active ingredient and impurities provided on Alternate CSF #2 were either established based on their respective averages derived from the five-batch preliminary analysis results or proposed for the 100% accountability.

Note: The registrant submitted the revised alternate CSF #2 (dated 01-05-2021), in which the registrant has corrected the certified limits for the AI by proposing standard certified limits for the active ingredient.

The product chemistry data submitted for Guideline 830.1750 satisfy the data requirements of 40 CFR §158.350.

830.1800 (enforcement analytical method)

The enforcement analytical method employed to quantify the active ingredient in Quizalofop P-ethyl Technical was HPLC-UV/DAD with external standard calibration, which was validated in terms of linearity, precision, and accuracy (MRID No. 51096402). The active ingredient was identified by using HPLC-DAD-MS, FT-IR, UV-Vis, and ^{1}H-NMR respectively against Quizalofop-P-ethyl analytical standard (MRID No. 51096402).

The analytical methods used to determine the amounts of the impurities were provided in MRID No. 51096402. (Refer to "830.1700 (preliminary analysis)" under section "Confidential Appendix" for a summary of the methods).

The product chemistry data submitted for Guideline 830.1800 satisfy the data requirements of 40 CFR §158.355.

2. Group B guidelines (physical-chemical properties):

No Group B product chemistry data are required for the current registration application as the product is already registered.

CONCLUSIONS:

The CITAB has reviewed the proposed Alternate CSF #2 (dated 04/02/2020) and the supporting Group A data for Quizalofop P-ethyl Technical and has concluded that:

1. The product chemistry data submitted for guidelines 830.1550 (product identity and composition), 830.1600 (description of materials used to produce the product), 830.1620 (description of production process), 830.1670 (discussion of the formation of impurities), 830.1700 (preliminary analysis), and 830.1800 (enforcement analytical method) are acceptable.

2. The data submitted for guideline 830.1750 (certified limits) require upgrading. No justification was provided for the expanded upper certified limit for the active ingredient.

3. The proposed revised Alternate CSF #2 (dated 01-05-202110 which will supersede the previously proposed alternate CSF #2 (dated 04/02/2020). The proposed revised alternate CSF #2 (dated January 5, 2021) is acceptable.

4. The product chemistry data for the Group B guidelines are not required for the current registration application as the product is already registered.

830.1550. Product identity & composition: (MRID No. 51096401)

Common Name: Quizalofop-P-ethyl

IUPAC Name: Ethyl (R)-2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propionate

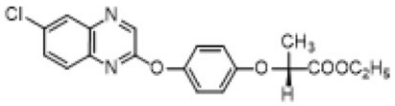
CAS Name: Not provided

CAS Number: 100646-51-3

Molecular formula: $C_{19}H_{17}ClN_2O_4$

Molecular weight: 372.8 g/mol

Structural formula:



Group A Product Chemistry Data

Table 1. Manufacturing and Impurity Data for "Quizalofop P-ethyl Technical"

GLN	Requirement	MRID	Status	Details and /or Deficiency
830.1550	Product Identity and composition	51096401	A	Adequately described
830.1600	Description of materials used to produce the product	51096401	A	SDSs and specifications of the starting materials were provided.
830.1620	Description of production process	51096401	A	A detailed description of the production process was provided.
830.1670	Discussion of formation of impurities	51096401	A	The origins of the impurities were provided.
830.1700	Preliminary analysis	51096402	A	A five-batch analysis of the active ingredient and impurities was conducted.
830.1750	Certified limits	51096401	A	The registrant proposed standard certified limits for the AI in the revised alt CSF #2 (dated 01-05-2021)
830.1800	Enforcement analytical method	51096402	A	The validated analytical method for quantifying the active ingredient was HPLC-UV/DAD.

A = Acceptable; N = Unacceptable (see Deficiency); N/A = Not Applicable; G = Data gap; I = In progress; U = Up-grade (additional information required);

830 Series Subgroup B (Physical-Chemical Properties)

No Group B product chemistry data are required for the current registration application as the product is already registered.

830.1800 (enforcement analytical method)
(MRID No. 51096402)

The active ingredient in Quizalofop P-ethyl Technical was quantified by HPLC-UV/DAD with external standard calibration (Method No. NC2016153A) (MRID Nos. 51096401 and 51096402). The method was validated for system suitability (chromatographic suitability and consistency of system performance), specificity, linearity, precision (repeatability) and accuracy (MRID No. 51096402). The identification for the active ingredient was performed by using HPLC-DAD-MS, FT-IR, UV-Vis and ^{1}H-NMR respectively against Quizalofop-P-ethyl analytical standard (MRID No. 51096402).

The samples of Quizalofop P-ethyl Technical were dissolved in hexane, and then separated by reverse phase HPLC using the following chromatographic conditions. The details for sample preparation were provided in MRID No. 51096402, pp. 40 and 105. The retention time for Quizalofop P-ethyl was approximately 12.0 minutes.

Instrument:	Agilent 1100/1200 series HPLC
HPLC Column:	CHIPALPAK AS-H 250 x 4.6 mm,5 µm
Mobile phase:	Hexane : iso-Propanol = 98:2 (V/V)
Column Temperature:	35 °C
Sample size injected:	5.0 µL
Stop time:	18.00 min
Flow rate:	1.40 mL/min.
Signal Wavelength:	240 nm
Signal BW:	4 nm
Reference Wavelength:	off
Reference BW:	off
Store spectra:	None (all for validation of specificity)

The concentration (% w/w) of the active ingredient in Quizalofop P-ethyl Technical was calculated by using the formula below.

Content of **Quizalofop-P-ethyl** (%) = (R/R') x (W '/ W) x ρ x 100

Where:

W '- mass of standard of the **Quizalofop-P-ethyl** (mg);

R - area of the **Quizalofop-P-ethyl** peak in **Quizalofop-P-ethyl TC** chromatograms;

W- mass of **Quizalofop-P-ethyl TC** (mg);

R'- average area of the **Quizalofop-P-ethyl** peak in two chromatograms of the standard solution bracketing the sample injection;

ρ- purity of the **Quizalofop-P-ethyl** standard (%)

A summary of the method validation data for quantifying the active ingredient is presented in the table below.

Components		**Results**[a]
Specificity		No interference peaks were noted around the retention time of Quizalofop P-ethyl.
Linearity of response	Correlation Coefficient	0.9996
	Range of Linearity	496.16 – 1527.91 mg/L
Precision (% RSD)		0.88 (less than the Horwitz value of 1.35) (n =6)
Accuracy (% Recovery)		99.2 ± 1.19
[a]Data are from MRID No. 51096402, pp. 32 – 38 of 116.		

Pages 8-22*Manufacturing process information may be entitled to confidential treatment*

DATA EVALUATION RECORD

Quizalofop P-ethyl Technical

STUDY TYPE: PRODUCT CHEMISTRY REVIEW

OCSPP 830.1550; 830.1600; 830.1620; 830.1670; 830.1700; 830.1750; 830.1800

MRIDS 51096401, 51096402

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Task Order No. Product Chem – 3-17b

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Summitec Corp. for the U.S. Environmental Protection Agency under Contract No. EP-W-16-019

Pages 24-25*Confidential Statement of Formula may be entitled to confidential treatment*